CLAIMS

WE CLAIM:

1. A composition for providing an artificial chemotactic factor gradient *in vivo* comprising one or more chemotactic factor(s).

2. A composition for providing an artificial chemotactic factor gradient *in vivo* comprising one or more chemotactic factor(s) and a device.

3. A composition for providing an artificial chemokine gradient *in vivo* comprising one or more chemokine(s).

4. A composition for providing an artificial chemokine gradient *in vivo* comprising one or more chemokine(s) and a device.

5. A composition for providing an artificial chemokine gradient *in vivo* comprising one or more chemokine(s) and ethylene-vinyl-acetate.

6. A composition for entrapping antigen presenting cells in a subject comprising one or more chemotactic factor(s); and one or more APC stimulating factor(s).

7. A composition for entrapping antigen presenting cells in a subject

comprising one or more chemokine(s) and one or more APC stimulating factor(s).

8. A composition for entrapping antigen presenting cells in a subject comprising one or more chemokine(s) and one or more reactive hapten(s).

9. A composition for loading antigen presenting cells in a subject comprising one or more chemotactic factor(s), one or more APC stimulating factor(s), and one or more immunoregulatory molecule wherein the immunoregulatory molecule is loaded into the antigen presenting cells.

10. A composition for regulating an immune response in a subject comprising one or more chemotactic factor(s), one or more APC stimulating factor(s), and one or more immunoregulatory molecule(s).

11. The composition of claim 1 or 3, 6, 7, 8, 9 or 10 further comprising a device.

12. The composition of claim 6, 9 or 10 wherein the chemotactic factor is incorporated into a device.

13. The composition of claim 8 wherein the chemokine is incorporated into a device.

14. The composition of claim 9 or 10 wherein the immunoregulatory molecule is incorporated into a device.

15. The composition of claim 9 or 10 wherein the chemotactic factor and the immunoregulatory molecule are incorporated into a device.

16. The composition of claim 11, 12, 13, 14 or 15 wherein the device is selected from the group consisting of nondegradable implant systems, biodegradable implant systems, implantable pump systems and atypical implantable pump systems.

17. The composition of claim 11, 12, 13, 14 or 15 wherein the nondegradable implant system is selected from the group consisting of polymeric matrix systems (monolitic systems); reservoir systems; and bead systems, such as polymethylmethacrylate (PMMA) and polydimethylalloxane (PDMS) beads.

18. The composition of claim 11, 12, 13, 14 or 15 wherein the biodegradable implant system is selected from the group consisting of reservoir systems; polymer monolitic systems, such as polyglycolic acid, polyactic acid, polyglycolic-lactic acid, polycaprolactone,

ethylene-vinyl-acetate and actic acid/lysine; biodegradable copolymers with nondegradable coatings, such as ethylene-vinyl-acetate/methacrylate.

19. The composition of claim 11, 12, 13, 14 or 15 wherein the implantable pump system is selected from the group consisting of infusion pumps, peristaltic pumps, osmotic pumps, positive displacement pumps and controlled release micropumps.

20. The composition of claim 11, 12, 13, 14 or 15 wherein the atypical implantable pump system is selected from the group consisting of ceramic composites, inorganic bone meal or ossograft, alminium calcium phosphorous oxide ceramics, hydroxyapetite ceramics, tricalcium phosphate and amino acid antibiotic composite ceramics, hydrogels, intraocular implants and transurethral systems.

21. The composition of claim 11, 12, 13, 14 or 15 wherein the device is ethylene-vinyl-acetate.

22. The composition of claim 1, 2, 6, 9 or 10 wherein the chemotactic factor is selected from the group consisting of chemokines, nucleotides and neuropeptides.

23. The composition of claim 3, 4, 5, 7, 8 or 22 wherein the chemokine is selected from the group consisting of MIP-1α, RANTES, MCP-3, MIP-5, MCPs, TARC, MDC,

MIP-3α, IL-8, SDF-1, MIP-3β and SLC.

24. The composition of claim 22 wherein the nucleotide is selected from the group consisting of ADP, UTP and UDP.

25. The composition of claim 22 wherein the neuropeptide is selected from the group consisting of calcitonin-related gene protein and α-melanocyte-stimulating hormone.

26. The composition of claim 3, 4, 5, 7, 8 or 22 wherein the chemokine is MIP-3β.

27. The composition of claim 6, 7, 9 or 10 wherein the APC stimulating factor is selected from the group consisting of reactive haptens; cytokines, bacterial products, and ultraviolet radiation.

28. The composition of claim 8 or 27 wherein the reactive hapten is selected from the group consisting of dinitroflourobenzene, fluorescein isothiocyanate, oxazolone and urushiol.

29. The composition of claim 27 wherein the cytokine is selected from the group consisting of tumor necrosis factor-α and Interleukin 1.

30. The composition of claim 27 wherein the bacterial product is selected from the group consisting of lipopolysacharrides and lipoproteins.

31. The composition of claim 9 or 10 wherein the immunoregulatory molecule is selected from the group consisting of antigens, immunostimulatory molecules and immunosuppressive molecules.

32. The composition of claim 31 wherein the antigen is selected from the group consisting of tumor-associated antigens, self antigens, allogeneic antigens, xenogeneic antigens and infectious disease-associated antigens.

33. The composition of claim 32 wherein the tumor-associated antigen is selected from the group consisting of immunoglobulin idiotype, TCR, mutant p21/*ras*, mutant p53, p210/ber-abl fusion product, MART-1/melan A, MAGE-1, the GAGE family, human papilloma virus antigen, Epstein Bar virus antigen, tyrosinase, gp100, prostatic acid phosphatase, prostatic-specific antigen, prostate-specific membrane antigen, thyroglobulin, telomerase, Her-2/neu, carcinoembryonic antigen, and Muc-1.

34. The composition of claim 31 wherein the immunostimulatory molecule is selected from the group consisting of cytokines, co-stimulatory receptors, and bacterial products.

35. The composition of claim 34 wherein the cytokine is selected from the group consisting of GM-CSF, interferon-α, interferon-β, interferon-γ, IL-1, IL-2, IL-6, IL-7, IL-12, IL-15 and TNFα.

36. The composition of claim 34 wherein the co-stimulatory receptor is selected from the group consisting of CD40 ligand and inducible co-stimulatory protein.

37. The composition of claim 34 wherein the bacterial product is selected from the group consisting of lipopolysacharrides and lipoproteins.

38. The composition of claim 31 wherein the immunosuppressive molecule is selected from the group consisting of cytokines, soluble co-stimulatory molecules, neuropeptides, death ligands, and immunosuppressive chemicals.

39. The composition of claim 38 wherein the cytokine is selected from the group consisting of IL-4, IL-10, IL16 and transforming growth factor-β.

40. The composition of claim 38 wherein the soluble co-stimulatory molecule is selected from the group consisting of cytotoxic T lymphocyte antigen 4-immunoglobulin , CD80-Ig, CD86-Ig and ICOS-Ig.

41. The composition of claim 38 wherein the neuropeptide is selected from the group consisting of CGRP and α-MSH.

42. The composition of claim 38 wherein the death ligand is selected from the group consisting of CD95 ligand and TRAIL.

43. The composition of claim 38 wherein the immunosuppressive chemical is selected from the group consisting of corticosteroids, cyclosporin A, and FK506.

44. A method for providing an artificial chemotactic factor gradient *in vivo* comprising one or more chemotactic factor(s).

45. A method for providing an artificial chemotactic factor gradient *in vivo* comprising one or more chemotactic factor(s) and a device.

46. A method for providing an artificial chemokine gradient *in vivo* comprising one or more chemokine(s).

47. A method for providing an artificial chemokine gradient *in vivo* comprising one or more chemokine(s) and a device.

48. A method for providing an artificial chemokine gradient *in vivo* comprising one or more chemokine(s) and ethylene-vinyl-acetate.

49. A method for entrapping antigen presenting cells in a subject comprising one or more chemotactic factor(s); and one or more APC stimulating factor(s).

50. A method for entrapping antigen presenting cells in a subject comprising one or more chemokine(s) and one or more APC stimulating factor(s).

51. A method for entrapping antigen presenting cells in a subject comprising one or more chemokine(s) and one or more reactive hapten(s).

52. A method for loading antigen presenting cells in a subject comprising one or more chemotactic factor(s), one or more APC stimulating factor(s), and one or more immunoregulatory molecule(s) wherein the immunoregulatory molecule is loaded into the antigen presenting cells.

53. A method for regulating an immune response in a subject comprising one or more chemotactic factor(s), one or more APC stimulating factor(s), and one or more immunoregulatory molecule(s).

54. The method of claim 44, 46, 49, 50, 51, 52 or 53 further comprising a device.

55. The method of claim 49, 52, 53 wherein the chemotactic factor is incorporated into a device.

56. The method of claim 51 wherein the chemokine is incorporated into a device.

57. The method of claim 52 or 53 wherein the immunoregulatory molecule is incorporated into a device.

58. The composition of claim 52 or 53 wherein the chemotactic factor and the immunoregulatory molecule are incorporated into a device.

59. The method of claim 54, 55, 56, 57 or 58 wherein the device is selected from the group consisting of nondegradable implant systems, biodegradable implant systems, implantable pump systems and atypical implantable pump systems.

60. The method of claim 54, 55, 56, 57 or 58 wherein the nondegradable implant system is selected from the group consisting of polymeric matrix systems (monolitic

systems); reservoir systems; and bead systems, such as polymethylmethacrylate (PMMA) and polydimethylalloxane (PDMS) beads.

61. The method of claim 54, 55, 56, 57 or 58 wherein the biodegradable implant system is selected from the group consisting of reservoir systems; polymer monolitic systems, such as polyglycolic acid, polyactic acid, polyglycolic-lactic acid, polycaprolactone, ethylene-vinyl-acetate and actic acid/lysine; biodegradable copolymers with nondegradable coatings, such as ethylene-vinyl-acetate/methacrylate.

62. The method of claim 54, 55, 56, 57 or 58 wherein the implantable pump system is selected from the group consisting of infusion pumps, peristaltic pumps, osmotic pumps, positive displacement pumps and controlled release micropumps.

63. The method of claim 54, 55, 56, 57 or 58 wherein the atypical implantable pump system is selected from the group consisting of ceramic composites, inorganic bone meal or ossograft, alminium calcium phosphorous oxide ceramics, hydroxyapetite ceramics, tricalcium phosphate and amino acid antibiotic composite ceramics, hydrogels, intraocular implants and transurethral systems.

64. The method of claim 54, 55, 56, 57 or 58 wherein the device is ethylene-vinyl-acetate.

65. The method of claim 44, 45, 49, 52 or 53 wherein the chemotactic factor is selected from the group consisting of chemokines, nucleotides and neuropeptides.

66. The method of claim 46, 47, 48, 50, 51 or 65 wherein the chemokine is selected from the group consisting of MIP-1α, RANTES, MCP-3, MIP-5, MCPs, TARC, MDC, MIP-3α, IL-8, SDF-1, MIP-3β and SLC.

67. The method of claim 65 wherein the nucleotide is selected from the group consisting of ADP, UTP and UDP.

68. The method of claim 65 wherein the neuropeptide is selected from the group consisting of calcitonin-related gene protein and α-melanocyte-stimulating hormone.

69. The method of claim 46, 47, 48, 50, 51 or 65 wherein the chemokine is MIP-3β.

70. The method of claim 49, 50, 52 or 53 wherein the APC stimulating factor is selected from the group consisting of reactive haptens; cytokines, bacterial products, and ultraviolet radiation.

71. The method of claim 51 or 70 wherein the reactive hapten is selected from

the group consisting of dinitroflourobenzene, fluorescein isothiocyanate, oxazolone and urushiol.

72. The method of claim 70 wherein the cytokine is selected from the group consisting of tumor necrosis factor-α and Interleukin 1.

73. The method of claim 70 wherein the bacterial product is selected from the group consisting of lipopolysacharrides and lipoproteins.

74. The method of claim 52 or 53 wherein the immunoregulatory molecule is selected from the group consisting of antigens, immunostimulatory molecules and immunosuppressive molecules.

75. The method of claim 74 wherein the antigen is selected from the group consisting of tumor-associated antigens, self antigens, allogeneic antigens, xenogeneic antigens and infectious disease-associated antigens.

76. The method of claim 75 wherein the tumor-associated antigen is selected from the group consisting of immunoglobulin idiotype, TCR, mutant p21/*ras*, mutant p53, p210/ber-abl fusion product, MART-1/melan A, MAGE-1, the GAGE family, human papilloma virus antigen, Epstein Bar virus antigen, tyrosinase, gp100, prostatic acid phosphatase, prostatic-

specific antigen, prostate-specific membrane antigen, thyroglobulin, Her-2/neu, carcinoembryonic antigen, telomerase and Muc-1.

77. The method of claim 74 wherein the immunostimulatory molecule is selected from the group consisting of cytokines, co-stimulatory receptors, and bacterial products.

78. The method of claim 77 wherein the cytokine is selected from the group consisting of GM-CSF, interferon-α, interferon-β, interferon-γ, IL-1, IL-2, IL-6, IL-7, IL-12, IL-15 and TNFα.

79. The method of claim 77 wherein the co-stimulatory receptor is selected from the group consisting of CD40 ligand and inducible co-stimulatory protein.

80. The method of claim 77 wherein the bacterial product is selected from the group consisting of lipopolysacharrides and lipoproteins.

81. The method of claim 74 wherein the immunosuppressive molecule is selected from the group consisting of cytokines, soluble co-stimulatory molecules, neuropeptides, death ligands, and immunosuppressive chemicals.

82. The method of claim 81 wherein the cytokine is selected from the group

consisting of IL-4, IL-10, IL16 and transforming growth factor-β.

83. The method of claim 81 wherein the soluble co-stimulatory molecule is selected from the group consisting of cytotoxic T lymphocyte antigen 4-immunoglobulin , CD80-Ig, CD86-Ig and ICOS-Ig.

84. The method of claim 81 wherein the neuropeptide is selected from the group consisting of CGRP and α-MSH.

85. The method of claim 81 wherein the death ligand is selected from the group consisting of CD95 ligand and TRAIL.

86. The method of claim 81 wherein the immunosuppressive chemical is selected from the group consisting of corticosteroids, cyclosporin A, and FK506.

87. A vaccine comprising one or more chemotactic factor(s), one or more APC stimulating factor(s), and one or more immunoregulatory molecule(s).

88. The vaccine of claim 87 wherein the chemotactic factor is selected from the group consisting of chemokines, nucleotides and neuropeptides.

89. The vaccine of claim 88 wherein the chemokine is selected from the group consisting of MIP-1α, RANTES, MCP-3, MIP-5, MCPs, TARC, MDC, MIP-3α, IL-8, SDF-1, MIP-3β and SLC. .

90. The vaccine of claim 88 wherein the nucleotide is selected from the group consisting of ADP, UTP and UDP.

91. The vaccine of claim 88 wherein the neuropeptide is selected from the group consisting of calcitonin-related gene protein and α-melanocyte-stimulating hormone.

92. The vaccine of claim 88 wherein the chemokine is MIP-3β

93. The vaccine of claim 87 wherein the APC stimulating factor is selected from the group consisting of reactive haptens, cytokines, bacterial products and ultraviolet radiation.

94. The vaccine of claim 93 wherein the reactive hapten is selected from the group consisting of dinitroflourobenzene, fluorescein isothiocyanate, oxazolone and urushiol.

95. The vaccine of claim 93 wherein the cytokine is selected from the group consisting of tumor necrosis factor-α and Interleukin 1.

96. The vaccine of claim 93 wherein the bacterial product is selected from the group consisting of lipopolysacharrides and lipoproteins.

97. The vaccine of claim 87 wherein the immunoregulatory molecule is selected from the group consisting of antigens, immunostimulatory molecules and immunosuppressive molecules.

98. The vaccine of claim 97 wherein the antigen is selected from the group consisting of self antigens, allogeneic antigens, xenogeneic antigens tumor-associated antigens and infectious disease-associated antigens.

99. The vaccine of claim 98 wherein the tumor-associated antigen is selected from the group consisting of immunoglobulin idiotype, TCR, mutant p21/*ras*, mutant p53, p210/ber-abl fusion product, MART-1/melan A, MAGE-1, the GAGE family, human papilloma virus antigen, Epstein Bar virus antigen, tyrosinase, gp100, prostatic acid phosphatase, prostatic-specific antigen, prostate-specific membrane antigen, thyroglobulin, Her-2/neu, carcinoembryonic antigen, telomerase and Muc-1.

100. The vaccine of claim97 wherein the immunostimulatory molecule is selected from the group consisting of cytokines, co-stimulatory receptors, and bacterial products.

101. The vaccine of claim 100 wherein the cytokine is selected from the group consisting of GM-CSF, interferon-α, interferon-β, interferon-γ, IL-1, IL-2, IL-6, IL-7, IL-12, IL-15 and TNFα.

102. The vaccine of claim 100 wherein the co-stimulatory receptor is selected from the group consisting of CD40 ligand and inducible co-stimulatory protein.

103. The vaccine of claim 100 wherein the bacterial product is selected from the group consisting of lipopolysacharrides and lipoproteins.

104. The vaccine of claim 97 wherein the immunosuppressive molecule is selected from the group consisting of cytokines, soluble co-stimulatory molecules, neuropeptides, death ligands, and immunosuppressive chemicals.

105. The vaccine of claim 104 wherein the cytokine is selected from the group consisting of IL-4, IL-10, IL16 and transforming growth factor-β.

106. The vaccine of claim 104 wherein the soluble co-stimulatory molecule is selected from the group consisting of cytotoxic T lymphocyte antigen 4-immunoglobulin , CD80-Ig, CD86-Ig and ICOS-Ig.

107. The vaccine of claim 104 wherein the neuropeptide is selected from the group consisting of CGRP and α-MSH.

108. The vaccine of claim 104 wherein the death ligand is selected from the group consisting of CD95 ligand and TRAIL.

109. The vaccine of claim 104 wherein the immunosuppressive chemical is selected from the group consisting of corticosteroids, cyclosporin A, and FK506.

110. The vaccine of claim 87 wherein the chemotactic factor is incorporated into a device.

111. The vaccine of claim 87 wherein the immunoregulatory molecule is incorporated into a device.

112. The vaccine of claim 87 wherein the chemotactic factor and the immunoregulatory molecule are incorporated into a device.

113. The vaccine of claims 110, 111 or 112 wherein the device is selected from the group consisting of is selected from the group consisting of nondegradable implant systems, biodegradable implant systems, implantable pump systems and atypical implantable pump

systems.

114. The vaccine of claim 113 wherein the nondegradable implant system is selected from the group consisting of polymeric matrix systems (monolitic systems); reservoir systems; and bead systems, such as polymethylmethacrylate (PMMA) and polydimethylalloxane (PDMS) beads.

115. The vaccine of claim 113 wherein the biodegradable implant system is selected from the group consisting of reservoir systems; polymer monolitic systems, such as polyglycolic acid, polyactic acid, polyglycolic-lactic acid, polycaprolactone, ethylene-vinyl-acetate and actic acid/lysine; biodegradable copolymers with nondegradable coatings, such as ethylene-vinyl-acetate/methacrylate.

116. The vaccine of claim 113 wherein the implantable pump system is selected from the group consisting of infusion pumps, peristaltic pumps, osmotic pumps, positive displacement pumps and controlled release micropumps.

117. The vaccine of claim 113 wherein the atypical implantable pump system is selected from the group consisting of ceramic composites, inorganic bone meal or ossograft, alminium calcium phosphorous oxide ceramics, hydroxyapetite ceramics, tricalcium phosphate and amino acid antibiotic composite ceramics, hydrogels, intraocular implants and transurethral

systems.

118. The vaccine of claim 113 wherein the device is ethylene-vinyl-acetate.

119. The vaccine of claim 87 wherein the loaded antigen presenting cells migrate to draining lymph nodes.

120. A method of regulating an immune response in a subject comprising administering to said subject the vaccine of claim 87 through 119.

121. The method of claim44, 45, 49, 52 or 53 wherein the chemotactic factor is administered subcutaneously.

122. The method of claim 49, 50, 52 or 53 wherein the APC stimulating factor is administered topically.

123. The method of claim 52 or 53 wherein the immunoregulatory molecule is administered subcutaneously.

124. The vaccine of claim 87 wherein the chemotactic factor is administered subcutaneously.

125. The vaccine of claim 87 wherein the APC stimulating factor is administered topically.

126. The vaccine of claim 87 wherein the immunoregulatory molecule is administered subcutaneously.

127. The composition of claim 32 wherein the self antigen is selected from the group consisting of Rh blood group antigens, platelet integrins, non-collangenous domain of basement membrane collagen type IV, epidermal cadherins, streptococcal cell-wall antigens, rheumatoid factor IgG complexes, DNA, histones, ribosomes, snRNP, scRNP, pancreatic beta-cell antigen, unknown synovial joint antigen, myelin basic protein, protolipid protein, and myelin oligodendrocyte glycoprotein.

128. The composition of claim 32 wherein the allogeneic antigen is selected from the group consisting of class I major histocompatability complex molecules, class II major histocompatability complex molecules, non-classical major histocompatability complex molecules and minor antigens.

129. The method of claim 75 wherein the self antigen is selected from the group consisting of Rh blood group antigens, platelet integrins, non-collagenous domain of basement membrane collagen type IV, epidermal cadherins, streptococcal cell-wall antigens,

rheumatoid factor IgG complexes, DNA, histones, ribosomes, snRNP, scRNP, pancreatic beta-cell antigen, unknown synovial joint antigen, myelin basic protein, protolipid protein, and myelin oligodendrocyte glycoprotein.

130. The method of claim 75 wherein the allogeneic antigen is selected from the group consisting of class I major histocompatability complex molecules, class II major histocompatability complex molecules, non-classical major histocompatability complex molecules and minor antigens.

131. The vaccine of claim 98 wherein the self antigen is selected from the group consisting of Rh blood group antigens, platelet integrins, non-collagenous domain of basement membrane collagen type IV, epidermal cadherins, stroptococcal cell-wall antigens, rheumatoid factor IgG complexes, DNA, histones, ribosomes, snRNP, scRNP, pancreatic beta-cell antigen, unknown synovial joint antigen, myelin basic protein, protolipid protein, and myelin oligodendrocyte glycoprotein.

132. The vaccine of claim 98 wherein the allogeneic antigen is selected from the group consisting of class I major histocompatability complex molecules, class II major histocompatability complex molecules, non-classical major histocompatability complex molecules and minor antigens.